From stem cells to schizophrenia in a dish

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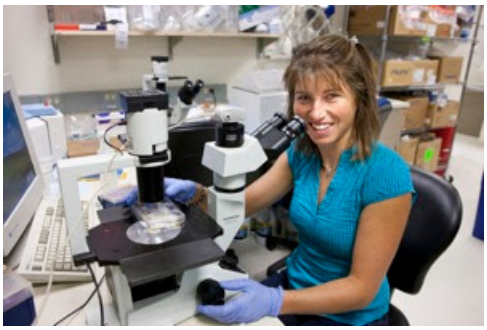

Kristen Brennand

CIRM grantee Fred Gage at The Salk Institute for Biological Studies and his lab are creating a veritable cellular hospital of disease conditions playing out in laboratory dishes. What they learn from these diseases-in-miniature could lead to new ways of creating and screening drugs to treat the disorder.

In 2008, he matured embryonic stem cells into the type of nerve cells damaged in ALS. This study led to insights in how the damage occurs and could provide a way of screening new drugs. Then in November of 2010, Gage and his colleagues published a paper in which they reprogrammed skin cells from people with a genetic form of autism spectrum disorders. They then matured those iPS cells into neurons that they could study in the lab.

Now, Gage and his team have published a paper in *Nature* in which they pulled off a similar feat, this time with schizophrenia. They took skin cells from people with a genetic form of the disease and reprogrammed those cells back to an embryonic-like state. They then matured those cells into neurons - neurons that produced significantly fewer connections than is normally seen. What's more, the drug Loxapine, used to treat schizophrenia, helped restore those connections. No other frequently prescribed antipsychotic medication was able to restore those connections.

A Salk press release quotes Fred Gage, who is professor in the Salk's Laboratory of Genetics and holder of the Vi and John Adler Chair for Research on Age-Related Neurodegenerative Diseases:

> "Schizophrenia exemplifies many of the research challenges posed by complex psychiatric disorders," says Gage. "Without a basic understanding of the causes and the pathophysiology of the disorder, we lack the tools to develop effective treatments or take preventive measures."

The group also found almost 600 genes whose activity was different between normal neurons and those from the schizophrenia cell. Roughly a quarter of those had been implicated in schizophrenia in the past.

The press release quoted Gage again:

> "For many years, mental illness has been thought of as a social or environmental disease, and many thought that if affected people just worked through their problems, they could overcome them," says Gage. "What we are showing are real biological dysfunctions in neurons that are independent of the environment."

We produced a video of Gage discussing the role of stem cells in understanding diseases:

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Nature, April 13, 2011

- A.A.

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